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(54) PHARMACEUTICAL COMBINATION

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(*) Notice:

This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

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(56)**References Cited**

U.S. PATENT DOCUMENTS

3,317,384	4		5/1967	Underwood 167/58
4,512,978	4		4/1985	Inwood 424/145
4,610,868 A	4		9/1986	Fountain et al 424/1.1
6,068,860 /	1	*	5/2000	Carlsson et al 424/601

FOREIGN PATENT DOCUMENTS

AU	0636255	* 5/1992	A61K/31/66
AU	636255	4/1993	A61K/31/66
EP	0350287	1/1990	A61K/31/70
EP	0594223	4/1994	A61K/31/70
WO	9219244	11/1992	A61K/31/57
wo	9503805	2/1995	A61K/31/52
wo	9527501	10/1995	A61K/38/21

OTHER PUBLICATIONS

Alenius, S., et al; Therapeutic Effects of Foscarnet Sodium and Acyclovir on Cutaneous Infections due to Herpes Simplex Virus Type 1 in Guinea Pigs, J. Inf. Dis. 1982; 145:569-73.

The Human Herpesviruses, ed. Roizman et al. 1993, Whitely, Richard et al.; The epidemiology and Clinical Manifestations of Herpes Smplex Virus Infections.

Kristofferson, A. et al.; Limited Efficacy of Inhibitors of Herpes Simplex Virus DNA Synthesis in Murine Models of Recrudescent Disease, J. Gen. Virol. (1988), 69, 1157-1166.

Schinazi, R.F. et al; Studies In Vitro and In Vivo of Combinations of Antivirals and Antiinflammatory Agents in Relation to the Treatment of Herpes Simplex Viruses, Current Chemotherapy and Immunotherapy, 12th Int. Congress, Florence, Jul. 1981.

From Chemical Abstracts, vol. 112, nr. CA:125021: Loftsson, T.; Effect of choline esters and oleic acid on the penetration of acyclovir, estradiol, hydrocortisone, nitroglycerin, retinoic acid and trifluorothymidine across hairless mouse skin in vitro, Acta Pharm. Nor. (1989), 1(5), 279-86.

From Chemical Abstracts, vol. 112, nr 4, (dissertation): Choi, Hoo Kyun: Enhanced transdermal delivery of propanolol, hydrocortisone, acyclovir and peptide-type drugs (1989).

Power, W J et al., Acyclovir ointment plus topical betamethasone or placebo in first episode disciform keratitis, British Journal of Ophtalmology 1992; 76:711-713.

McGill, J. Herpes zoster ocular infection, Scand. J. Infect. Dis. Suppl. 46: 85-88, 1985.

ABPI Compendium of Data Sheets and Summaries of Product Characteristics, 1996-97, Datapharm Publications Ltd., pp. 390 and 1271.

Berkow, et al., The Merck Manual of Diagnosis and Therapy, 14th Edition, pp. 2023-2025 (1982).

Chemical Abstract No. 97: 156002r from Schinazi, et al., Curr. Chemother. Immunother. 2, 1085-1087 (1982).*

Merck Index 10th Ed #140, #4135, #1435, 1984.*

Notter et al, 89 CA:157769t, 1978.*#jf139##

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ABSTRACT (57)

The invention relates to pharmaceutical compositions for topical administration comprising a topically acceptable antiviral substance and an antiinflammatory glucocorticoid in a pharmaceutically acceptable carrier. The pharmaceutical composition can be used in the prophylactic and curative treatment of herpesvirus infections in mammals including man. The invention also relates to the use of a combination of a topically acceptable antiviral substance and an antiinflammatory glucocorticoid for the manufacture of a medicament for said prophylactic and curative treatment.

36 Claims, 3 Drawing Sheets